New Computational Approach Accelerates Drug and Therapy Discovery for Intrinsically Disordered Proteins

New Qeios preprint presents ISM-SM, a computational method to identify small-molecule candidates for intrinsically disordered proteins

BELGRADE, SERBIA, November 14, 2025 /EINPresswire.com/ -- A new study introduces a computational framework that may help researchers identify small molecules capable of modulating intrinsically disordered proteins (IDPs) — a class of biomolecules that have long been considered elusive to traditional drug discovery.
The work, published as an open peer-reviewed preprint on the open-science platform Qeios, describes the Informational Spectrum Method for Small Molecules (ISM-SM), developed by Dr Milan Senćanski, Principal Research Fellow at the Vinča Institute of Nuclear Sciences, a National Institute of the Republic of Serbia, affiliated with the University of Belgrade.

A Challenge in Drug Discovery
Intrinsically disordered proteins, which lack stable three-dimensional structures, play critical roles in neurodegenerative diseases, viral pathogenesis, and cancer. Their dynamic nature prevents the reliable identification of fixed binding pockets, making conventional docking-based or structure-guided drug design approaches difficult to apply.
The ISM-SM method offers an alternative pathway. By applying Electron-Ion Interaction Potential (EIIP) parameters and information spectrum analysis, ISM-SM characterises both protein sequences and small molecules based on their long-range electronic properties. The method allows the prediction of potential interactions without relying on a single, rigid protein structure.

Informational Spectrum Method for Small Molecules (ISM-SM)
The ISM-SM approach extends the principles of the Informational Spectrum Method (ISM), previously used to study protein-protein and protein-virus interactions, to small molecules.
In this model, biological sequences and chemical structures are transformed into digital signals representing their electron-distribution characteristics. The resulting spectra are compared to identify compatible frequencies that signify potential long-range recognition between a protein and a molecule.
In the presented preprint, the ISM-SM workflow is applied to a representative intrinsically disordered target. The analysis demonstrates that the method can discriminate between compounds with high and low predicted relevance, effectively filtering promising candidates for

further in silico and experimental evaluation.
This computational protocol is compatible with drug repurposing pipelines and can be integrated with molecular docking or molecular dynamics simulations for refinement.

Results and Implications
The study highlights several outcomes:
• Identification of spectral compatibility between specific small molecules and the target IDP, indicating possible interaction potential.
• Feasibility of long-range interaction modelling even in the absence of a defined tertiary structure.
• Applicability to large chemical libraries, enabling rapid, low-cost virtual screening of both novel and approved compounds.
The approach is intended as a first-pass filter to prioritise molecules before structural or biochemical assays, thereby reducing the experimental search space.
The findings support the broader idea that electronic descriptors can provide meaningful insight into biomolecular recognition beyond spatial docking constraints.
In this context, ISM-SM provides a new analytical layer that complements existing computational methods.

Open Peer Review on Qeios
The article has undergone open peer review on the Qeios platform, where all reviews and author responses are publicly available.
This transparent evaluation process aligns with the open-science principles increasingly adopted by the international research community, ensuring that methodological details and interpretations are openly discussed and refined.
The preprint is accessible at: https://www.qeios.com/read/5DGYBH.2

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